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CASE BASED REVIEW

SAPHO: has the time come for tailored therapy?

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Abstract

SAPHO (synovitis, acne, pustulosis, hyperostosis and osteitis) syndrome is a heterogeneous condition combining osteoarticular and cutaneous manifestations. Conventional treatments are mostly ineffective. We hereby report two patients, the first with an aggressive form of disease and the second with an incomplete response to two different anti-TNF-α agents. Both were successfully treated with tocilizumab and ustekinumab, respectively, over a long period of time. A narrative review of a biological therapy in SAPHO syndrome yielded very little information on the specific use of these agents. We highlight the advantages of personalising therapy and describe emerging promising treatments for this disease.

Keywords Anti-IL-1 agents · Anti-IL-12/IL-23 agents · Anti-IL-6 agents · Anti-TNF-α agents · SAPHO syndrome · Treatment

Introduction

Synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO) syndrome is a rare chronic immune-mediated condition characterised by combined osteoarticular and cutaneous manifestations [1]. Not every patient presents with the full spectrum of the disease [2]. Given its heterogeneity, diagnosis is challenging and conventional treatments, ranging from non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, antibiotics and bisphosphonates to several disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate, sulfasalazine or azathioprine, have yielded suboptimal responses [3, 4]. Anti-tumour necrosis factor-alpha (anti-TNF-α) agents and interleukin-1 (IL-1) antagonists have achieved more effective outcomes but some patients remain refractory and may only respond in a single organ domain [4, 5]. There is scarce information on the value of more recent biological response modifier therapies.

We first describe the follow-up of two patients with SAPHO syndrome treated with tocilizumab and ustekinumab, respectively. We then review all previous studies involving patients with SAPHO treated with biological agents, synthetic agents and cell signalling pathway inhibitors, with a special focus on non-anti-TNF-α agents, with respect to therapeutic outcome. We suggest the current array of biological therapies allows for the treatment of SAPHO patients in a personalised fashion, aiming to achieve early remission and preventing irreversible organ damage.

Methods

Demographic data, clinical records, therapeutic options and outcomes in patients treated with biological agents were the focus of the case reports and literature review. The latter was performed in a narrative form, through a PubMed search, using the terms "SAPHO" and "syndrome" and "treatment", up until the 31st December 2018, with no other publication date constraints. Additional relevant literature was hand-picked. The search was performed by two authors and resulted in a total of 324 articles. The first selection was restricted to manuscripts written in English, French, Spanish and Portuguese but only manuscripts written in English were found. Patient reports in review articles were included but we rejected editorials, commentaries, congress presentations and articles reporting SAPHO patients not exposed to biological therapies.

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Then, chronologically, we selected every single publication reporting clinical cases that described SAPHO syndrome patients subjected to biologicals and more recent compounds, obtaining a total of 40 manuscripts (11 single-centre cohort and 29 single case reports) as illustrated in the flowchart (Fig. 1). Mendeley was used as the reference manager. Duplicate information regarding individual patients was resolved. While the present study was being conducted, a series of 45 SAPHO patients subjected to biological therapy was published [6]. We found 22 additional cases and separately analysed biological non-TNF-α therapy-treated patients, the latter constituting our main research focus.

There is no unified concept of remission in SAPHO syndrome. When all organ systems ameliorate, response is generally considered complete. When response to therapy is dichotomized into cutaneous or articular, it is considered partial, according to symptomatic relief and irrespective of organ damage.

Results

Patient 1 case report

In 2001, a 27-year-old male, HLA B27 negative, complained of severe sternoclavicular and left arm pain for several years. Imaging showed bilateral clavicular and left humerus osteosclerosis and hyperostosis; concordantly, bone scintigraphy revealed increased uptake in both first sternocostal and sternoclavicular joints and middle third of the humeral shaft. Of note, the patient had suffered from severe acne vulgaris (face and trunk) from the age of 15, treated intermittently with doxycycline and isotretinoin with resolution of cutaneous manifestations. Combined NSAIDs, calcium supplementation, alendronate, weekly methotrexate (MTX), up to 25 mg per week, and prednisolone (10 mg per day) failed to provide pain relief, preventing him from working for a period of approximately 5 years. A regimen of intravenous tocilizumab (TCZ), 8 mg/kg per month, was attempted in 2011 and resulted in complete clinical remission for the next 8 years, up to the present time. Follow-up bone scintigraphy (2018) showed improvement (Fig. 2). Despite erosive changes (Fig. 3), the patient has been pain free and able to cope with a full-time employment since TCZ onset. He refused switching to subcutaneous formulation of TCZ and continues monthly therapy.

Patient 2 case report

In 2000, a 41-year-old female, HLA B27 negative, presented with severe sternoclavicular joint synovitis. She suffered from palmoplantar pustulosis for the past 15 years which worsened during the previous year with polyarthralgia of the wrists, elbows, shoulders and proximal interphalangeal, metacarpophalangeal and tibiotarsal joints. She started NSAID and weekly MTX up to 20 mg per week, with mild clinical improvement of the peripheral joints but no improvement regarding skin manifestations and anterior chest pain. Bone scintigraphy showed in-

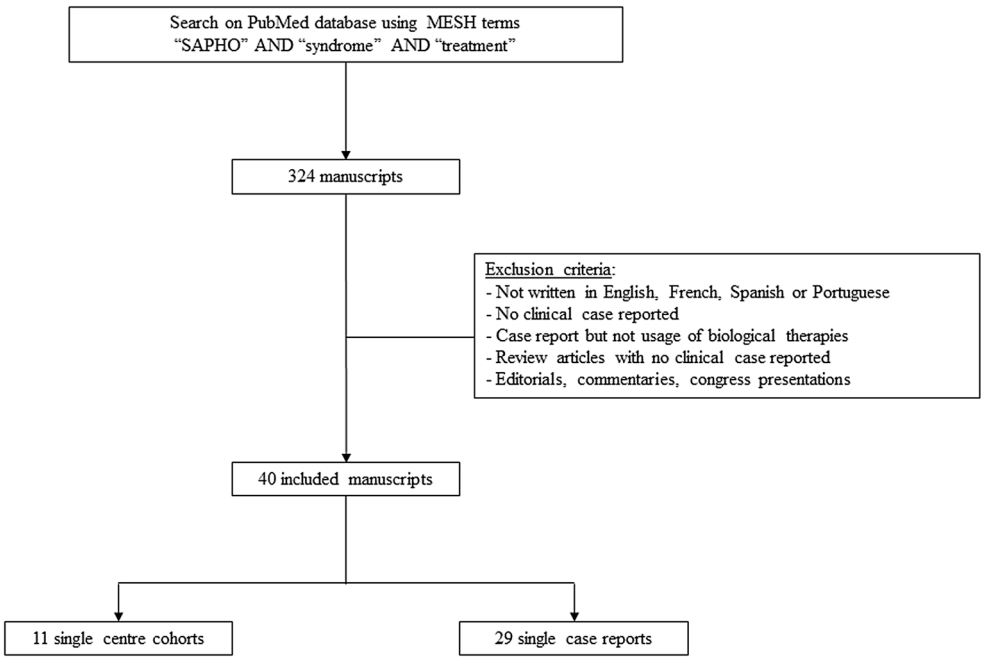

Fig. 1 Literature review methodology flowchart

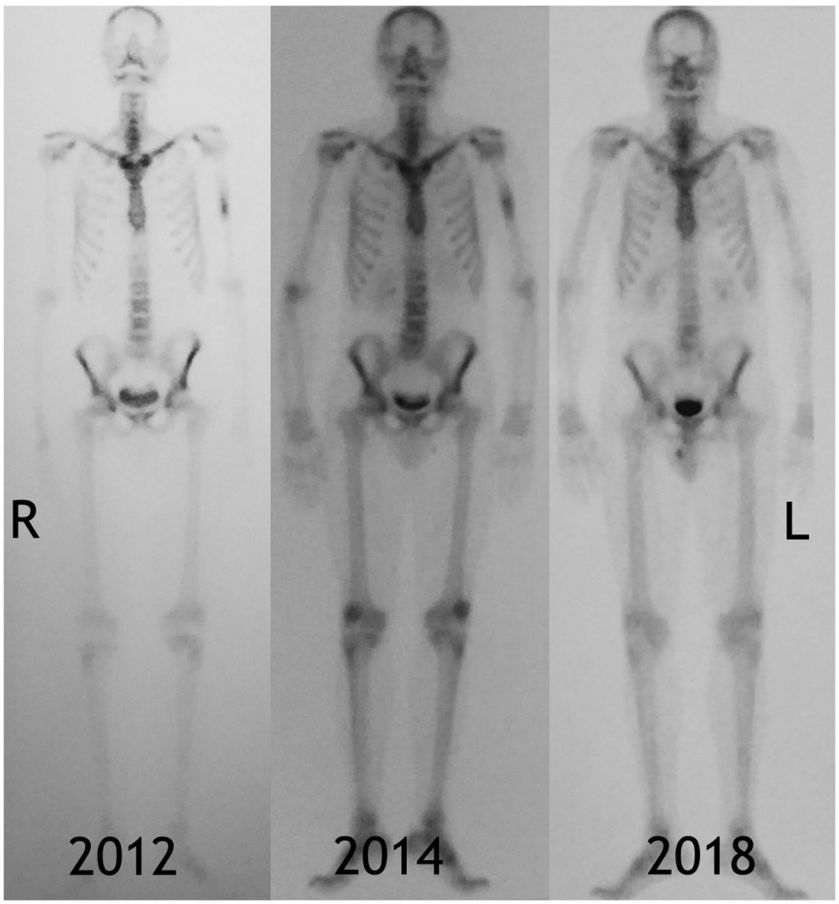

Fig. 2 Sequential bone scintigraphy: Initial bone scintigraphy images were obtained 2 h after radiolabelled injection. There is increased uptake in the middle third of the humeral shaft, sternocostal and sternoclavicular joints, with much less intensity at follow-up. L = left; R = right

creased uptake on both sternoclavicular joints, first right rib and first left sternocostal joint. In December 2011, a regimen of adalimumab 40 mg every 2 weeks in addition to MTX was prescribed and provided symptomatic relief. However, the treatment had to be interrupted after 2 months due to new onset scalp psoriasis with severe alopecia.

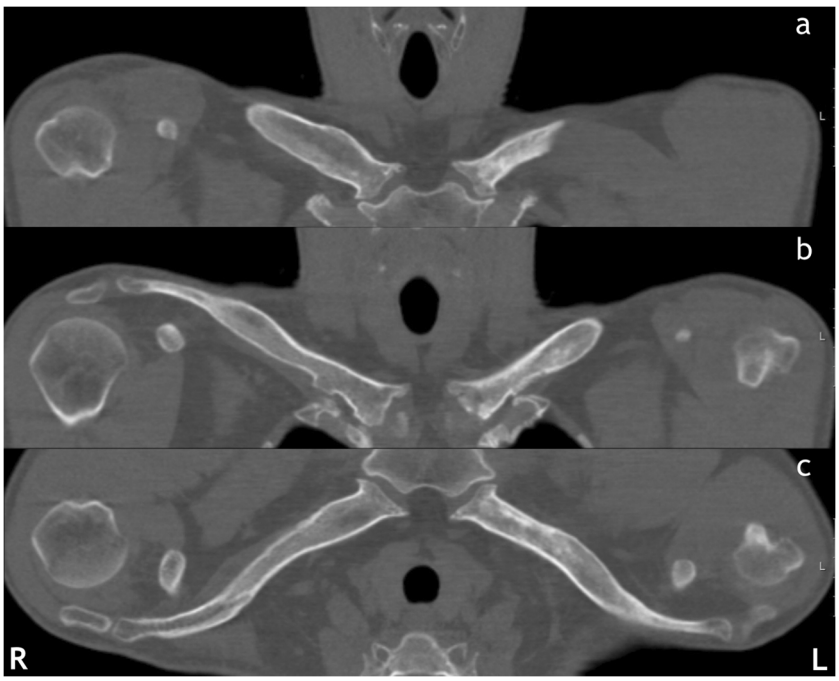

Fig. 3 Computerised tomography multiplanar reconstruction at the shoulder girdle level. Para-coronal views show sternoclavicular (**a**) and costoclavicular (**b**) joint erosion with marginal osteophytosis on the clavicle side, accompanied by joint space narrowing; para-axial views reveal diffuse osteosclerosis and mild hyperostosis affecting the middle third of both clavicles, more pronounced on the left (c). L = left; R = right

Treatment was switched from May 2012 to etanercept 50 mg per week, providing intermittent improvement of joint pain but failure to resolve palmoplantar pustulosis. A switch to ustekinumab was made in March 2016, resulting in symptomatic sustained cutaneous and articular disease complete remission with discontinuation of MTX over the next 3 years (Figs. 4 and 5).

Elevated serum markers of inflammation (C-reactive protein and ESR) normalised in both patients. Neither patient experienced side effects.

Literature review

Our literature review found a total of 67 patients treated with biological therapies. We selected eight manuscripts which described a total of 19 case reports of SAPHO syndrome for which non-TNF-α and recently developed agents including targeted synthetic DMARDs were used. Data extraction concerning every single patient found in the literature was exhaustively documented according to a pre-defined protocol. As outlined in Table 1, most patients reported were female ($N = 14$; 74%) with a mean age similar between females and males (43.2 ± 11 and 43.2 ± 14, respectively). Except for 2 patients (#15 and #16), osteoarticular and cutaneous manifestations occurred in every patient, 15 of whom presented with palmoplantar pustulosis. Overall, anakinra, ustekinumab, secukinumab and tocilizumab were successful in patients who were refractory to prior NSAID, corticosteroid, conventional DMARDs (cDMARDs), pamidronate and anti-TNF-α therapy. Of note, patients #12 and #14 failed to respond to two classes of biological DMARDs (bDMARDs); patient #17 was refractory to three different classes of bDMARDs and was rescued by apremilast; tofacitinib was also successful in a single patient (#18). Mean time from diagnosis to final treatment was only reported for 13 patients and was highly variable (8 ± 6 years). After a mean follow-up of 8 ± 6 months, only four patients had failed to achieve clinical remission (#7, 9, 10, 14).

We pooled all patients that ever switched to a second biological therapy ($n = 18$), consisting of those that switched between anti-TNF-α drugs ($n = 5$) and another group that switched to a different class of biological agent ($n = 13$, 12 taken from Table 1). Full remission was described in 72% ($n = 13/18$), three patients failing to respond and two patients only achieving partial remission. Of note, novel or aggravating cutaneous reactions occurred in 8 patients (44%) and these were described with every class of bDMARD (Table 2). Paradoxical psoriasis reactions were observed in 2 patients (one under ustekinumab and another under secukinumab–#9 and 14). A third patient had a local reaction after an etanercept injection and a pustular skin rash consistent with a drug hypersensitivity reaction during secukinumab treatment. Four patients under infliximab treatment had cutaneous reactions namely a skin flare, allergic urticaria, a psoriatic rash and worsening of palmoplantar pustulosis lesions that resolved after treatment discontinuation. A single patient developed an aseptic abscess during tocilizumab treatment remaining unclear whether this was an adverse event or a complication of SAPHO syndrome.

The remaining 42 patients subjected to therapy with a single anti-TNF-α comprised 14 males and 28 females (Table 3). Mean age was slightly higher in females than males (42.4 ± 12 and 35.1 ± 11, respectively). Mean follow-up was 16.8 ± 25 months and most patients were treated with infliximab ($n = 23$) followed by etanercept ($n = 11$), adalimumab ($n = 7$) and certolizumab pegol ($n = 1$). They had been followed for an average of 17 months, the longest having been in partial remission, on infliximab, for 11 years. Every patient had osteoarticular manifestations. Overall, complete, partial or no remissions were observed in 30, 10 and 2 patients respectively. For those patients with both osteoarticular and cutaneous manifestations ($n = 35$), the

Fig. 4 Plantar pustulosis during etanercept treatment (**a**) and after ustekinumab (**b**)

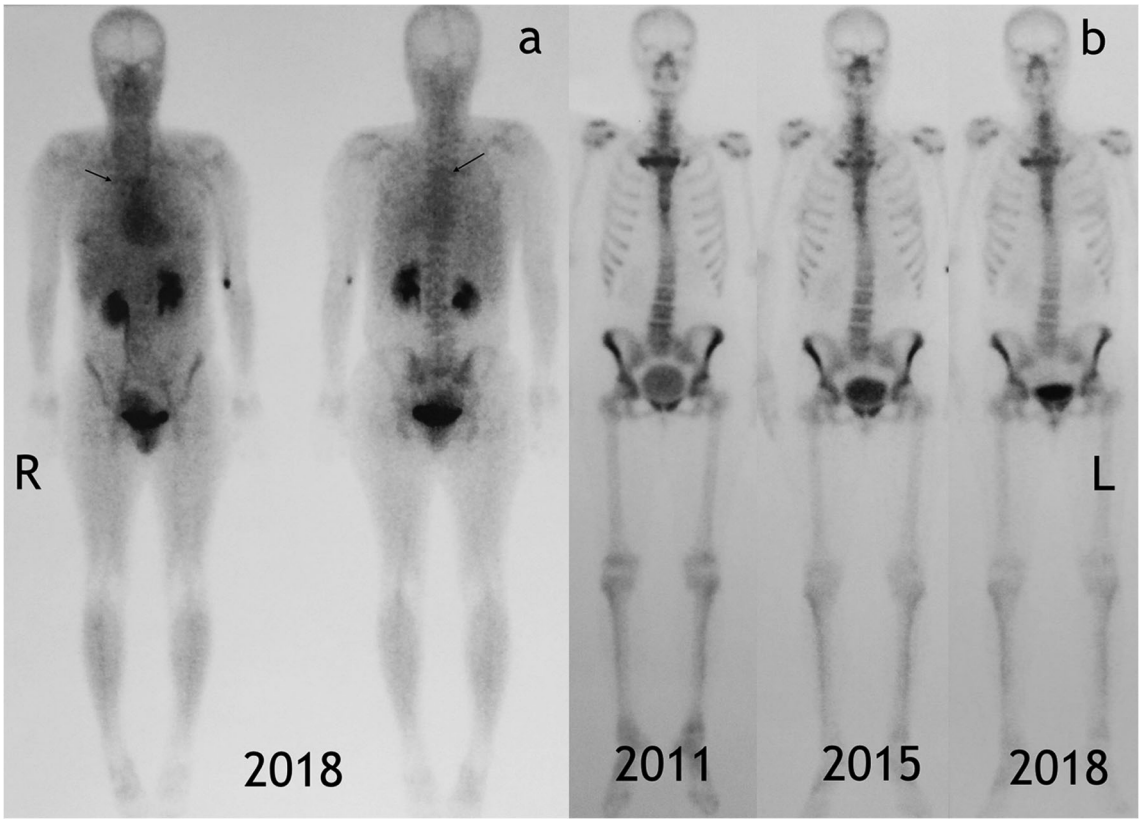

Fig. 5 Sequential bone scintigraphy: Images obtained 5 min after intravenous injection of technetium-99m demonstrates slightly increased uptake (arrow) at the sternocostal joint of the first rib on the right, anterior and posterior views (arrows) (a); 2 h after injection there is increased uptake at the medial surface of the first right rib, sternoclavicular joints and left sternocostal joint of the first rib with progressive reduction over an eight-year follow-up (b); R = right; L = left

presence of cutaneous manifestations was not associated to a lack of response to anti-TNF-α agents, and 24 of such patients (69%) were considered complete responders. There was no statistically significant therapeutic benefit associated to therapy with either infliximab or etanercept. Significantly, partial remissions to anti-TNF-α therapy were always due to a lack of response in the cutaneous domain, corresponding to 10/35 patients (29%).

Discussion and conclusions

SAPHO syndrome is rare; there are no controlled clinical trials and its aetiology and pathogenesis remains unknown. In general, as SAPHO is a heterogeneous condition, a lack of specific evaluation tools—as regards to both global and organ-specific disease activity and damage—hampers classification of treatment responses. The narrative review highlights the wide variety of pharmacological therapies that have been attempted to treat SAPHO and suggests that the rationale behind each treatment is based on refractoriness to a previous therapy and/or availability of a new class of drug.

Approximately half of the anti-TNF-α-treated patients ($n = 21$) were reported between 2012 and 2015, after which time only six patients were described. Anti-IL-1 therapy was used as early as 2010 in a single patient, and in a case series of five patients in 2012 but generally overlooked thereafter. Use of other non-anti-TNF-α is described from 2016, underlying the younger age group of those treated with more recently marketed bDMARDs and targeted synthetic DMARDs. Lack of response to anti-TNF-α therapy was described with respect to SAPHO patients presenting with cutaneous manifestations, most frequently with palmoplantar pustulosis. This is in stark contrast with the overwhelming success of diverse non-anti-TNFα therapies, namely anakinra, ustekinumab, secukinumab, tocilizumab, tofacitinib and apremilast. While using a single database may be considered a limitation to the literature review, our strengths remain with the fact that we have undertaken the longest case-based review on SAPHO syndrome and the first focusing non-anti-TNFα therapies.

Our two case reports mirror the literature review with respect to a long delay from diagnosis to onset of effective therapy but highlight an important difference. The first patient had highly active osteoarticular disease and damage (erosions,

Table 1 SAPHO syndrome case reports treated with non-anti-TNF-α biological agents, describing clinical manifestations, follow-up and therapeutic outcomes

Reference/ Publication (y)	#	Age (y)	Sex	Osteoarticular features	Skin manifestations	Previous treatments	Time lapse (y)†	Final treatment	Follow-up (months)	Outcome
Colina [7]/2010	1	47	F	Manubrium and sternoclavicular osteitis, right knee synovitis	PPP, acne conglobata	SSZ	0.92	ANK	24	CR
Wendling [8]/2012	2	54	F	Synovitis and dactylitis	PPP	NSAIDs, PDN, MTX, LEF	11	ANK	6	CR
	3	41	M	Vertebral osteitis and synovitis	PPP	NSAIDs, PDN, colchicine, SSZ, retinoids	23	ANK	5	CR
	4	49	F	Synovitis	Hidradenitis suppurativa	NSAIDs, MTX, INF, retinoids	13	ANK	6	CR
	5	53	F	Pelvic osteitis and synovitis	PPP, furunculosis	NSAIDs, PDN, MTX, colchicine, INF, ETN, ADA	4	ANK	8	CR
	6	25	F	Synovitis, hyperostosis and osteitis	PPP	NSAIDs, pamidronate	2	ANK	6	CR
	7	37	M	Sternocostoclavicular osteitis and hyperostosis	PPP	NSAIDs, pamidronate, ADA, ETN	NA	ANK	5	NR
Cornillier [9]/2016	8	44	F	Axial and sternoclavicular arthritis	PPP, IGD	MTX, ETN, ADA, LEF	10	UST	3	CR
Wendling [10]/2017	9	37	F	ACW, axial and peripheral arthritis	PPP	MTX, pamidronate, ADA, INF	NA	UST	6	NR
	10	32	F	Axial and ACW arthritis	PPP, acne vulgaris	MTX, ADA	NA	UST	6	NR
	11	61	F	Arthritis	PPP	MTX, cyclosporine	10	UST	12	CR
	12	37	F	ACW, axial and peripheral arthritis	PPP	MTX, ADA, INF, UST	3	SEC	3	PR
	13	64	M	ACW, axial and peripheral arthritis	PPP	MTX, SSZ, INF, ADA	5	SEC	3	CR
	14	46	F	ACW and axial arthritis	PPP	MTX, SSZ, INF, ANK	NA	SEC	3	NR
Sato [11]/2017	15	48	M	Tibial osteosclerosis, humeral hyperostosis, CRMO	None	PDN, SSZ, colchicine, MTX, minodronate, NSAIDs	10	TCZ	4	CR
	16	26	M	Peripheral arthritis, tibial hyperostosis, CRMO	None	MTX, PDN, colchicine	2	TCZ	10	CR
Adamo [12]/2018	17	24	F	Osteitis, sternoclavicular and vertebral arthritis	PPP	Topical steroids, NSAIDs, M-PDN, MTX, SSZ, ETN, UST, ADA, SEC	NA	APR	23	CR
Yang [13]/2018	18	44	F	ACW and wrist synovitis	PPP	NSAIDs, MTX, IM-GC, hydroxychloroquine, ETN	NA	TFC	3	CR
Daoussis [6]/2018	19	53	F	ACW and shoulder arthritis	PPP	NSAIDs, zoledronic acid, MTX, steroids, INF, ADA	7	SEC	9	CR

y, year(s); #, patient number; *F*, female; *M*, male; *NA*, not available; *ACW*, anterior chest wall; *PPP*, palmoplantar pustulosis; *IGD*, interstitial granulomatous dermatitis; *SSZ*, sulfasalazine; *NSAIDs*, non-steroidal anti-inflammatory drugs; *PDN*, prednisone; *MTX*, methotrexate; *LEF*, leflunomide; *M-PDN*, methyl-prednisolone; *IM-GC*, intramuscular injection of glucocorticoids; *ANK*, anakinra; *INF*, infliximab; *ETN*, etanercept; *ADA*, adalimumab; *TCZ*, tocilizumab; *UST*, ustekinumab; *SEC*, secukinumab; *APR*, apremilast; *TFC*, tofacitinib; *CR*, complete remission; *PR*, partial remission; *NR*, no remission

†time elapsed between diagnosis and final treatment

Table 2 SAPHO syndrome patients subjected to switch between biological agents, describing rationale for switching and therapeutic outcomes

Reference	# in Table 1	Previous biological agent	Rationale for switching between biologicals	Final treatment	Outcome
Wendling [8]	5	INF	Lack of response	ANK	CR
	6	INF, ETN, ADA	Lack of response	ANK	CR
	7	ADA, ETN	Lack of response	ANK	NR
Cornillier [9]	8	ETN, ADA	Lack of response	UST	CR
Wendling [10	9	ADA, INF	Lack of response	UST	NR
	10	ADA	Lack of response	UST	NR
	12	ADA, INF, UST	Lack of response	SEC	PR
	13	INF, ADA	Lack of response	SEC	CR
	14	INF, ANK	Lack of response	SEC	NR
Adamo [12]	17	ETN, UST, ADA, SEC	ETN–local reaction to ETN; UST–upper airway infections; ADA–PPP flare; SEC–pustular skin rash	APR	CR
Yang [13]	18	ETN	Lack of response	TFC	CR
Daoussis [6]	19	INF, ADA	Lack of response	SEC	CR
Wagner [14]	–	INF	Bronchospasm	ETN	CR
Abdelghani [15]	–	INF	INF–osteoarticular and skin flare	ETN	CR
	–	INF	INF–allergic urticarial reaction	ADA	PR
	–	INF	INF–psoriatic rash	ETN	CR
Arias-Santiago [16]	–	INF	INF–worsening of skin lesions	ADA	CR
Fujita [17]	–	TCZ	TCZ–aseptic abcess	INF	CR

#, patient number; *PPP*, palmoplantar pustulosis; *INF*, infliximab; *ETN*, etanercept; *ADA*, adalimumab; *TCZ*, tocilizumab; *UST*, ustekinumab; *SEC*, seccucinumab; *ANK*, anakinra; *APR*, apremilast; *TFC*, tofacitinib; *CR*, complete remission; *PR*, partial remission; *NR*, no remission

hyperostosis and osteitis) that severely impacted his daily activities and the disease was non-responsive to longstanding MTX. Tocilizumab was chosen on the basis of its effect on inhibition of osteoclast activity [46] and even though delayed implementation failed to prevent irreversible joint damage, therapy proved to be highly effective. Palmoplantar pustulosis, refractory to anti-TNF-α therapy in the second patient, was treated with ustekinumab, based on reports of its efficacy specifically regarding palmoplantar psoriasis [47] and psoriatic arthritis [48]. While we recognise that both tocilizumab and ustekinumab had become commercially available at the time treatments were started, the rationale behind their successful use must be emphasised. Both therapies were chosen to target specific clinical manifestations. Moreover, in both patients, drug survival was maintained throughout the follow-up.

Paradoxical skin lesions such as palmoplantar pustulosis may be difficult to distinguish from a psoriatic rash just as both may be due to a flare of SAPHO syndrome or induced by anti-TNF therapy [49]. Of note, in the literature review, adverse cutaneous reactions were considered to represent exacerbations or lesions of a paradoxical nature, in three and five patients, respectively. In every single case, agent discontinuation was followed by a switch to an alternative bDMARD, akin to the course of action taken when the second patient developed severe scalp psoriasis.

Until the time comes for treatment to be based on scientific judgement, our case reports and literature review suggest that, in a manner similar to the latest recommendations for systemic rheumatic and cutaneous conditions [50], patients who are unresponsive to cDMARDs should be offered early biological therapy, tailored to the prevailing clinical phenotype. Analysis of the appropriateness of therapy in SAPHO syndrome seems jeopardized owing to the absence of dedicated scores to describe global disease activity and severity of clinical osteoarticular and cutaneous manifestations. In addition, strict definitions of remission for each organ domain need to be developed. Patients with SAPHO should be carefully observed for paradoxical and adverse cutaneous events and furthermore biologicals should be switched in order to achieve the lowest possible disease activity and prevent irreversible damage. Finally, we wish to underline that SAPHO may be a severely prolonged incapacitating condition, reinforcing a recommendation to avoid therapeutic delay and highlighting the ongoing challenge of a treat to target approach. Our case reports illustrate the successful use of biological therapies chosen on the basis of specific clinical manifestations and the longest known follow-up in clinical remission for tocilizumab and ustekinumab in SAPHO syndrome.

Table 3 SAPHO syndrome clinical case reports treated with anti-TNF-α agents

Reference/ publication (y)	Age (y)	Sex	Osteoarticular features	Skin manifestations	Final treatment	Follow-up (months)	Outcome
Olivieri [18] /2002	35	M	Left clavicular osteitis	Acne vulgaris	INF	18	CR
	52	M	Sternal, sternoclavicular joints, clavicular and rib osteitis	PPP	INF	18	CR
Wagner [14] /2002	44	F	DSOM	PPP	ETN	9	CR
Iqbal [19] /2005	23	M	Vertebral and clavicular osteitis	Acne fulminans	INF	10	PR
Massara [20] /2006	47	M	Sternoclavicular osteitis	PPP	INF	14	PR
	43	M	Sternoclavicular hyperostosis, bilateral sacroiliitis	PPP	INF	14	PR
	67	F	Right clavicular hyperostosis, peripheral arthritis	None	INF	8	CR
	42	F	Sternoclavicular hyperostosis, vertebral osteitis	PPP	INF	8	CR
Sabugo [21] /2007	39	M	Sternoclavicular osteitis	PPP	INF	NA	CR
Moll [22] /2008	45	F	Right ilium osteitis, sternoclavicular hyperostosis	PPP	INF	1.5	PR
	28	F	Right ilium osteitis	PPP	INF	15	PR
Fruehauf [23] /2009	43	F	Sternoclavicular and manubrium osteitis	Hidradenitis suppurativa	INF	10	PR
Castellví [24] /2010	28	F	Sternoclavicular osteitis, right sided sacroiliitis	PPP	ADA	17	CR
Vilar-Alejo [25] /2010	47	M	Axial and peripheral arthritis, wrist and elbow synovitis	Acne conglobata, hidradenitis suppurativa	ETN	32	CR
Souza [26] /2011	22	M	Peripheral arthritis	Hidradenitis suppurativa, acne vulgaris	INF	12	CR
Zhang [27] /2012	56	F	Vertebral and sternoclavicular osteitis	PPP	ETN	3	CR
Garcovich [28] /2012	25	M	Sternoclavicular, sternocostal and sacroiliac synovitis	Acne conglobata	ADA	24	CR
Burgemeister [29] /2012	25	F	Sternoclavicular synovitis	PPP, hidradenitis suppurativa	INF	1.5	CR
	44	F	Costochondral junction and sternoclavicular osteitis	PPP	INF	NA	CR
	37	F	Pubis osteitis	PPP and hidradenitis suppurativa	INF	NA	CR
Hampton [30] /2013	42	F	Shoulder and knee synovitis, costochondral and sternoclavicular involvement	None	INF	6	CR
Naves [31] /2013*	25	F	Sacroiliitis and chondrosternal hyperostosis	None	ADA	12	CR
	22	F	Clavicular and sternal sclerosis	Psoriasis	INF	96	CR
	41	F	Sacroiliitis and sternal sclerosis and hyperostosis	PPP, psoriasis	INF	132	PR
Kundu [32] /2013*	42	M	Manubrium, vertebra and sacro-iliac erosions	None	INF	NA	NR
Kim [33] /2014*	50	F	Sternoclavicular hyperostosis and sternal osteitis	PPP	INF	24	CR
Abourazzak [34] /2014	30	M	Clavicular osteitis and hyperostosis	PPP	ETN	12	CR
Marí [35] /2014	23	F	DSOM	Acne-like skin lesions, hidradenitis and psoriasis	ETN	NA	CR
Anić [36] /2014	18	M	Sternoclavicular arthritis	Acne vulgaris	ETN	18	PR
Sáez-Martín [37] /2015	39	F	Sternocostoclavicular arthritis, sacroiliitis, and feet osteitis	PPP and pustular psoriasis plaques	ETN	3	CR
Kamata [38] /2015	55	F	Bilateral clavicular, sternocostoclavicular and sternal hyperostosis	PPP	CTP	2	CR

Table 3 (continued)

Reference/ publication (y)	Age (y)	Sex	Osteoarticular features	Skin manifestations	Final treatment	Follow-up (months)	Outcome
Cotti [39] /2015	44	F	Clavicular hyperostosis, mandible sclerosis	None	ADA	6	CR
Su [40] /2015	42	M	Skull, sternocostoclavicular, manubrium, mandible, tibia and fibula osteitis	Acne vulgaris	ETN	6	PR
Abdelghani [15] /2015	58	F	Vertebral osteitis	PPP	INF	7	CR
	61	F	Manubrium osteitis, sacroiliac hyperostosis and osteosclerosis	None	ADA	24	CR
	53	F	Clavicular, rib and manubrium hyperostosis and osteosclerosis	None	ETN	1	CR
Zhang [41] /2016	33	F	Sternoclavicular and sacroiliac arthritis	PPP	ETN	0.75	CR
	29	F	Sternoclavicular and sacroiliac arthritis, discitis	PPP	ETN	1	CR
Mateo [42] /2017	53	F	Vertebral osteitis	PPP	INF	15	PR
Anić [43] /2017	48	F	Sternoclavicular, sternal and ribs osteitis	PPP	INF	4	CR
Cianci [44] /2017	53	F	Sternoclavicular and tibial osteitis	Pustular lesions on right gluteus	ADA	24	NR
Vekic [45] /2018	26	M	Sternal, scapular, peripheral and axial lesions, pubis hyperostosis	Pyoderma gangrenosum and acne vulgaris	ADA	14	CR

*additional cases; *y*, years; *F*, female; *M*, male; *DSOM*, diffuse sclerosing osteomyelitis of the mandible; *PPP*, palmoplantar pustulosis; *INF*, infliximab; *ETN*, etanercept; *ADA*, adalimumab; *CTP*, certolizumab pegol; *NA*, not available; *CR*, complete remission; *PR*, partial remission; *NR*, no remission

Compliance with ethical standards

Disclosures None.

Consent Both patients gave informed consent for the publication of their case report and related images.

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